IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF TEXAS
HOUSTON DIVISION

BEN N. BROWN, SR. Plaintiff VS. SHELL OIL COMPANY, SHELL CHEMICAL, L.P., RADIATOR SPECIALTY COMPANY, AND JOHN DOES 1 THROUGH 250, INCLUSIVE Defendants	§ § § § § § § § § § § §	C.A. NO. 4:08-CV-00413

DECLARATION

1. I, John W. Spencer, have over three decades of field experience in assessing and evaluating workers' exposure to hazardous agents, including benzene. For more than 32 years I have worked in the field performing industrial hygiene services for private clients and for government agencies. In doing so, I always identified and evaluated all possible routes of exposure to the workers at issue (which includes dermal exposure), and then worked with various personnel to manage and control these exposures. As a result, I have become one of the leaders in the industrial hygiene community.[1]

I am a member of the American Conference of Governmental Industrial Hygienists (ACGIH), the American Industrial Hygiene Association (AIHA), the American Board of Industrial Hygiene, the Board of Certified Safety Specialists, the Society for Chemical Hazard Communication, the New York Academy of Sciences, and was a member of the AIHA Product Health and Safety Committee and AIHA Emergency Response Planning Committee.

I have presented many times at the American Industrial Hygiene Conference, including presentations on the limitations of conducting dermal absorption modeling for volatile substances such as benzene.[2] I have published several articles in peer-reviewed journals on airborne exposure modeling and assessment. In these papers, I have discussed the value ***and limitations*** of exposure assessment models. I co-authored one such paper with Plaintiff's retained exposure expert, Mark Nicas, PhD ("Nicas").

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1 Past President of the Chesapeake Section of the American Industrial Hygiene Association.

2 "Dermal Modeling for Solvents – The Limitation of Applications for Practicing Industrial Hygienists" American Industrial Hygiene Conference and Exposition, Toronto, Canada. June 2009.

Exhibit C

2. Regarding Dr. Nicas' most recent expert report (dated June 15, 2009), I did not receive this new report until **August 4, 2009**. My report, and the opinions contained therein, was completed back on **March 6, 2009**. There was no way for me to address in the month of March something I did not receive until August.

3. All models must be validated before they can be reliably used in the real world. This involves, among other things, comparing the predictions calculated or generated by a model to actual, real world testing (actual measurements using validated methods). I do not deny that exposure models, including dermal exposure models, are in the published literature. In my opinion, dermal exposure models have been useful for qualitative analysis and for generating hypotheses and critical thinking within our scientific discipline.

However, using a model to quantify dermal exposures, and then comparing the results generated by that model to the occupational health standards is totally invalid. This "procedure" is not a generally-accepted industrial hygiene practice and has no real-world application as it relates to the determination of a given individual's exposure. Further the quantification of dermal dose is neither promulgated nor applied by the occupational health-related agencies.

Consider the National Institution for Occupational Safety and Health (NIOSH), which is the leading occupational safety and health research agency in the world as a part of the Public Health Service. NIOSH has literally conducted thousands of health hazard evaluations (HHE) for individual workers across the entire spectrum of American industry. While dermal exposures exist in the workplace, and while dermal exposures have certainly been recognized by OSHA and NIOSH, dermal exposures have neither been quantified nor subsequently "added to" inhalation exposures in the thousands of HHEs performed by NIOSH. Likewise, OSHA, the agency charged with regulating industry and worker exposures, has never conducted a quantification of dermal dose and cited an employer for overexposure for a benzene-related activity.

4. For benzene, the routine and generally accepted industrial hygiene practice is to (1) measure airborne concentrations, and (2) establish practices, policies and procedures to reduce or eliminate both inhalation and dermal routes of exposure. Outside the area of civil litigation, industrial hygienists do not quantify benzene dermal exposures for comparison to occupational health standards.[3] That is simply not done.

5. On several occasions in the context of litigation, I have been asked to comment on dermal dose estimates presented by an opposing expert (just like Nicas). On a few occasions, when asked, I have corrected the input parameters used by the opposing expert and have estimated a dermal dose using the opposing expert's "formula." The purpose of those exercises was to demonstrate what happens when one carefully and appropriately

3 Deposition of Dr. Mark Nicas in the case of Connie Lea Gibson Andrews vs. United States Steel Corporation; Case number D-504-CV-200601258; Fifth Judicial District Court in the state of New Mexico in the County of Chavez (page 179, lines 14-21).

selects input criteria. In that context, one has to understand the various parameters that go into using the formula and the selection of those parameters as being relevant and representative of the case at hand. I know how to use various models and understand the issues for using models to determine an individual's estimated exposure retrospectively.

The fundamental premise of industrial hygiene is "that science and art devoted to the anticipation, recognition, evaluation, and control of those environmental factors or stresses arising in or from the workplace, which may cause sickness, impaired health and well-being, or significant discomfort among workers or among the citizens of the community."[4] The industrial hygienist can thus give an expert opinion as to the degree of risk posed by the environmental stresses.

6. Under the current and long-standing regulatory and non-regulatory occupational health standards, *i.e.*, Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs), American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), and the National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limits (RELs), a separate dermal exposure limit for benzene does not exist. None of the above bodies require or recommend quantifying dermal exposures, and none of them provide or publish an accepted or validated method for comparing calculated modeled results with the health standards.

7. When formulating the current benzene standard, OSHA openly acknowledged the potential for benzene to be absorbed through the skin and recognized that route of exposure.[5] However, OSHA did not incorporate a separate dermal dose in the occupational health standard 29 CFR 1910.1028. The groups developing the benzene health standard used the inhalation dose as the surrogate for both inhalation and dermal routes of exposure. Plaintiff fails to mention or reference the primary studies[6,7,8,9,10,11]

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4 National Safety Council, "Fundamentals of Industrial Hygiene, Third Edition, page 3, 1988.

5 OSHA Preamble to the Benzene Standard September 11, 1987, page 34505.

6 Bond et al. "An update of mortality among chemical workers exposed to benzene." British Journal of Industrial medicine 43(1986): 685-691. [Note: Bond 1986 updated Ott 1978].

7 Infante PF, Rinsky RA, Wagonea JK, and Young RJ. "Leukemia in benzene workers." The Lancet (July 9, 1977): 76-78.

8 Ott MG, Townsend JC, Fishbeck WA, Langner RA. "Mortality among individuals occupationally exposed to benzene." Archives of Environmental Health (January/February 1978): 3-10.

9 Rinsky RA, Young RJ, and Smith AB. "Leukemia in Benzene Workers" American Journal of Industrial Medicine 2 (1981): 217-245. [Note: Rinsky et al 1981 "completed the follow-up begun by Infante et al 1977"].

10 Rinsky et al. "Benzene and Leukemia: An epidemiologic risk assessment. Cincinnati, OH: National Institute for Occupational Health and Safety. 1986.

that went into the development of the current occupational health standard which recognized the potential for dermal absorption but do not quantify the dermal component.

When evaluating the epidemiology (and to a lesser extent animal studies) that formed the basis for the occupational health standards, the dermal exposures of the workers under study were openly recognized. The dermal exposures were also essentially "captured" by the health standard because the health risk estimates were based on quantified inhalation exposures. If one assumes that the Pliofilm workers' actual exposures were slightly higher than the estimated doses based only on their inhalation (higher due to unquantified and unquantifiable dermal exposures), then the inhalation exposure limits (*i.e.*, the PELs) are slightly over-protective. If both routes of exposure (inhalation and dermal) were quantified then the result would have been a higher health standard than currently exists. The dose that the health standards are designed to protect against (~45 ppm years) is based on the epidemiology that demonstrated statistically significant increased risk at or above those doses. The doses were based on inhalation only. Therefore, if one assumes that the doses were actually higher (due to dermal exposure), then there is no reason to incorporate a dermal component. This is why putative dermal doses were never "added back" to the inhalation dose when these standards were developed.

While other regulatory agencies, including the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), and others, have established dermal models, only OSHA and the ACGIH have health standards and guidelines that are used to evaluate worker exposure in the relevant workplace environment.

8. I have explained in my report how and why the dermal flux value (the rate at which a material penetrates the skin) for a given solvent in a product mixture is too variable to be reliable. Dermal flux is uniquely dependent upon (1) other materials in the mixture, (2) relative percentages of each material in the mixture, and (3) environmental factors such as air speed across the skin surface, evaporation rates, and temperature.

9. Dermal flux is directly impacted by each of the following variables:

(a) the percentage of benzene in the mixture or material at issue;
(b) the presence and type of co-solvents ;
(c) ventilation rates;
(d) variation in evaporative losses at different skin temperatures;
(e) skin condition (wet/dry) or (intact/damaged);
(f) skin exposure location (i.e., palm, forearm, stomach, back, thigh);
(g) exposure frequency (i.e., single or repeated doses within a 4-hour time frame);
(h) inter-individual differences based on normal variation in human skin.

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11 Wong O. "An industry-wide mortality study of chemical workers occupationally exposed to benzene. Submitted to CMA, December 8, 1983. OSHA Docket Ho59B, exhibit 151-a.

The above-listed factors can raise or lower the flux estimate. Additionally, the rate of flux changes throughout the duration of the exposure event – *i.e.*, it is not fixed value.[12,13,14,15,16,17,18,19,20,21]

10. Plaintiff claims that I have not offered reasons why the data used by Dr. Nicas is incorrect. In my report (and again above) I have pointed out that the formula is not the issue *per se*. Rather, it is the application of the formula in this context, plus the input parameters that are the issue (*e.g.*, the flux value). In my report I explain:

> "Dr. Nicas' extrapolation of a flux value from pure benzene to predict a flux value for reformate containing various hydrocarbon chemicals including benzene has not been determined or validated, has no known error rate and is therefore unreliable. This approach does not address the differences in exposures based on personal factors (individual differences) nor does it address factors associated with the exposure environment (environmental factors such as temperature, airflow across the skin surface, etc.). Most significantly, his equation does not reflect the differences in flux based on the solvent (product) vehicle (formulation) or combination of other chemicals in the mixture."

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12 Arfsten, et al. "Characterization of the skin penetration of a hydrocarbon-based weapons maintenance oil." Journal of Occupational and Environmental Hygiene 3 (2006): 457-464.

13 Blank, I.H., and D. J. McAuliffe. "Penetration of Benzene Through Human Skin." J. Invest. Dermatol. 85 (1985): 522-526.

14 Boman, A. and Maibach, H.I. "Influence of Evaporation and Solvent Mixtures in the Absorption of Toluene and n-butanol in Human Skin in vitro." Annals of Occupational Hygiene 44 (2000): 125-135.

15 Hanke, J., T. Dutkiewicz, and J. Piotrowski. 1961. "The Absorption of Benzene Through the Skin in Man." Med. Pracy. 12 (1961): 413-426.

16 Loden, M. "The in vitro Permeability of Human Skin to Benzene, Ethylene Glycol, Formaldehyde, and n-Hexane." Acta Pharmacol. et Toxocol. 58 (1986): 382-389.

17 Maibach, H. I., and D.M. Anjo. "Percutaneous penetration of benzene and benzene contained in solvents used in the rubber industry." Archives of Environmental Health 36.5 (1981): 256-260.

18 McDougal, J.N. et al. "Dermal Absorption of Organic Chemical Vapors in Rats and Humans." Fundamental and Applied Toxicology 14 (1990): 299-308.

19 Nakai, J.S. et al. "Effect of Environmental Conditions on Penetration of Benzene through Human Skin." Journal of Toxicology and Environmental Health 51 (1997): 447-462.

20 Susten, et. al. "Percutaneous Penetration of Benzene in Hairless Mice: an Estimate of Dermal Exposure During Tire Building Operations." American Journal of Industrial Medicine 7 (1985): 323-335.

21 Craeber, JC. "USS Chemicals' Raffinate." Summary of analyses dated May 25, 1977. Bates stamp USS 10.

I went on to note:

> "Dr. Nicas did not consider the evaporation of benzene from reformate over time and assumes a constant concentration of benzene in reformate. However, he assumed that there was an airborne exposure to the benzene evaporating from reformate during this activity. Therefore, the estimated absorbed dose that Dr. Nicas converted to an airborne equivalent 8-hour TWA concentration and then added to his inhalation concentration estimate was not a reliable estimate of Mr. Brown's dermal or total benzene exposure. Finally, there is no standard or accepted method utilized by OSHA, NIOSH or the ACGIH for adding dermal dose to the measured airborne concentration for comparison with occupational health standards and guidelines."

11. Plaintiff Ben Brown has raised objections to the opinions I provided in my report. Plaintiff first states that I did not construct or use a dermal exposure model in the instant case. That is of course true. I did not "calculate" a dermal dose in this case using a model (as Nicas did) because such a procedure is well beyond the generally accepted industrial hygiene practice. First, the value that such a calculation might generate has no occupational health standard by which to compare. There is also no reference, text, or guidance by which one could compare its relevance. Second, the use of dermal models, including the one presented by Dr. Nicas, have only one real world value, which is that they can be used qualitatively to determine if additional workplace controls are needed to limit exposure. These models cannot be used, however, in the way that Dr. Nicas uses them. ***They cannot be employed to quantify an individual's benzene exposure in a workplace setting for comparison with occupational health standards.***

12. Plaintiff writes "[Spencer] tacitly admitted that he does not know how to perform mathematical modeling in that in thirty (30) years of working, allegedly monitoring benzene, he has not performed a dermal absorption calculation." This is incorrect. My knowledge of exposure modeling, which is extensive, has nothing to do with my opinion that Nicas' methodology is unreliable. It is true that I have never conducted a dermal absorption calculation for evaluating a real-world exposures. To do so would have amounted to unacceptable guesswork. In this small way, Dr. Nicas and I have the same opinion and are in total agreement as to the unreliability of this methodology.[22]

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22 *See FN* 3: May 9, 2008 sworn testimony of Dr. Nicas in *Andrews vs. U.S. Steel*:

> **Q.** During the time that you worked as an industrial hygienist throughout your career, how many times did you ever calculate a worker's dermal exposure in the course of giving an employer advice about limiting its worker's exposures?
> **Nicas.** I don't think I ever calculated a dermal exposure. It was more like you need to prevent dermal exposure. (pg 180)
> **Q.** How many times did you also tell the employer and, oh, by the way, in addition to these inhalation exposures, I've also separately calculated these dermal exposures your workers are getting. Did you ever do that?
> **Nicas.** I don't recall doing that. (pg 181)

13. Plaintiff writes "[Spencer's] definition of having done a dermal exposure measurement, is not taking the measurements; rather, it is, 'I know how to plug numbers into a model.'" I cannot decipher Plaintiff's specific criticism, nor is it clear to me what is meant by "not taking the measurements." On the next page of the deposition from which Plaintiff is citing, I testified as follows:

> **If we are concerned about dermal dose in addition to inhalation dose, we collect biological samples, blood or urine samples and have that evaluated, and that's why we do not use a dermal calculation to determine the significance of exposure.**[23]

This is, of course, consistent with the standard and generally accepted industrial hygiene practice. This practice comes from the ACGIH. ACGIH has established Biological Exposure Indices (BEIs) for comparison of quantified absorbed benzene (via actual biologic samples).[24] Currently, this is the only approved method for determining an absorbed dose of benzene.

It is true that one cannot conduct a retrospective assessment of an individual by way of biological monitoring, yet this practical limitation does not open the door for someone to use a methodology that is not generally accepted, not validated in the peer-reviewed literature, speculative and unreliable – *i.e.*, dermal modeling.

14. Plaintiff also writes that Spencer "just plugs number[s] into a model." I am unsure if this is meant as a criticism, for that is precisely what Plaintiff's expert (Dr. Nicas) has done in this case. Nicas did not develop his model for estimating a dermal dose. He simply "plugs in numbers" to generate a value for the alleged dermal dose.

15. I have no professional disagreement with the fact that the model exists, and have described how a model can be useful. It is the application of the model and the input parameters that matter. In this lawsuit, the model is not being used to make a qualitative judgment or inform an overall industrial hygiene evaluation. In this case, the model is being used to retrospectively calculate a dose. That methodology is totally unreliable, and as explained above and below, at odds with good science.

16. The input parameters or variables used by Dr. Nicas in this case demonstrate its unreliability. For example, for the "flux value" (which is the rate at which the material at issue penetrates the skin), Nicas relied on one and only one study conducted in Poland in 1961. Much more current studies[25,26,27,28,29] have also measured the rate at which benzene

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23 Deposition of John Spencer in the case of "Jo Ann Bishop, et al., vs. Shell Oil Co., et al." United States District Court Eastern District of Louisiana, case number is 07-2832. Page 23.

24 ACGIH TLV Committee. "Benzene." Documentation of the TLVs and BEIs. ACGIH Press, Akron, Ohio (2001) pp Benzene BEI -1 to 14.

25 Fiserova-Bergerova V and Pierce JT. "Biological Monitoring V: Dermal Absorption." Applied Industrial Hygiene, 4 (1989): F-14 - F-21.

is absorbed through the skin. The flux values reported in these more recent studies demonstrate that the actual flux for benzene is (1) widely variable and (2) dependant on many different factors. The variability of benzene flux is the first reason why "dose" values generated by Nicas' model are unreliable.[30,31,32]

17. Nicas co-authored a study where exposure to several organic solvents was evaluated in the workplace.[33] The brake-cleaning work under study involved potential dermal exposure to the solvents used to clean brakes (the authors personally observed the workers using latex gloves and recommended the use of more solvent resistant gloves). Nicas and his co-authors did not assess the dermal contribution to the workers' overall exposure, and no dermal dose quantification was presented. Only inhalation exposures were addressed in estimating worker exposures. Nicas and his co-authors also did not mention the need to assess the low levels of benzene contaminant in these degreasing solvents.

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26 Blank, I.H., and D. J. McAuliffe. "Penetration of Benzene through Human Skin." J. Invest. Dermatol, 85 (1985): 522-526.

27 Adami, et al. "Penetration of benzene, toluene and xylenes contained in gasolines through human abdominal skin in vitro." Toxicology in Vitro, 20 (2006): 1321-1230.

28 Franz, TJ. Chapter 5 "Percutaneous Absorption of Benzene." In Advances in Modern Environmental Toxicology. Volume VI – Applied Toxicology of Petroleum Hydrocarbons. Editors: MacFarland, Holdsworth, MacGregor, Call, and Lane. Princeton Scientific Publications, Inc. 1984: 61-70.

29 Loden, M. "The in vitro Permeability of Human Skin to Benzene, Ethylene Glycol, Formaldehyde, and n-Hexane." Acta Pharmacol. et Toxicol., 58 (1986): 382-389.

30 Franz stated, "further work is needed ...to define the role of vehicle (solvents or mixtures other than pure benzene) in controlling percutaneous absorption of benzene." Ibid 5

31 Bowman and Maibach 2000 commented, "Industrial exposure is also often to mixtures and seldom to the neat compound or solvent. If one or several compounds are volatile, evaporative loss of one or several of these can dramatically change the absorption of the others as their relative concentrations are increased. Many organic solvents have a high vapour pressure and can be expected to have a substantial loss through evaporation when non- occluded skin is exposed." Boman, A. and Maibach, H.I. "Influence of Evaporation and Solvent Mixtures in the Absorption of Toluene and n-butanol in Human Skin in vitro." Annals of Occupational Hygiene, 44 (2000) pages 131, 133.

32 Riviere, JE and Brooks, JD. "Prediction of dermal absorption from complex chemical mixtures: incorporation of vehicle effects and interactions into a QSPR framework." SAR and QSAR in Environmental Research, 18 (2007):1, 31 — 44.

33 Wilson, Michael P., Hammond, S. Katharine, Nicas, Mark and Hubbard, Alan E. , 'Worker Exposure to Volatile Organic Compounds in the Vehicle Repair Industry', Journal of Occupational and Environmental Hygiene, 4:5, 301 – 310, 2007.

In the Ben Brown lawsuit, where organic solvent exposure is alleged to be a key issue, Nicas quantifies Plaintiff's dermal exposure using a model. By contrast, in his peer-reviewed study of workers with dermal exposure to organic solvents, Nicas and his co-authors did no such thing.

18. I have personally collaborated with Dr. Nicas on the application of mathematical inhalation models as a tool for exposure assessment.[34] The purpose of these studies was to attempt to validate certain models by comparing predicted findings with actual results based on accepted air monitoring and analytical techniques. This collaborative investigation dealt with air modeling and inhalation exposures.

19. OSHA, ACGIH, and NIOSH have not established a validated formula or method for determining dermal dose by use of any model. In the preamble to the benzene standard, OSHA presented a discussion regarding the evaluation and assessment of dermal exposures.

20. Plaintiff writes that I provided no basis for my critique that Nicas used "inappropriate air monitoring data to be representative of Mr. Brown's airborne exposure."[35] On the contrary, I addressed in some detail this unreliable assessment by Nicas on page 9, paragraphs three (3) and four (4) of my report. I note that Nicas has since removed this methodological error from his assessment.

21. Plaintiff mentions research published by Dennis Paustenbach, PhD, even though Paustenbach did not develop the formula or model in question. Plaintiff writes that Paustenbach's work in the "Reconstruction of Benzene Exposure for the Pliofilm Cohort (1936-1976) Using Monte Carlo Techniques"[36] is the basis or foundation that supports Nicas' use of the flux formula for calculating dermal dose. Yet in the very article cited by Plaintiff, Paustenbach writes:

> **The new estimates presented in this analysis incorporate what is considered to be the most likely range of plausible exposure values, and, accordingly, provide a better characterization of the potential workplace exposure for this cohort. These data could be combined with current or future mortality information to calculate a new cancer potency factor or occupational health standard for benzene."**

As explained above, if one incorporates a dermal component into the evaluation of worker exposures for comparison with occupational health standards, a new standard would need to be developed.

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34 Nicas, M, Plisko, M.J., Spencer, J.W., "Estimating Benzene Exposure at a Solvent Parts Washer" Journal of Occ. and Env. Hygiene, 2006.

35 John Spencer Rebuttal Report in the Ben Brown vs Shell Oil et al., dated 6 March 2009.

36 Williams, P.R.D., Paustenbach, D. J., "Reconstruction of Benzene Exposure for the Pliofilm Cohort (1936-1976) Using Monte Carlo Techniques," Journal of Toxicology and Env. Health, 2003.

22. A key variable used in Nicas' formula is the dermal flux or rate at which the material passes through the skin. As Paustenbach pointed out in his paper, "The estimate of benzene uptake rate is one of the most important (and contentious) parameters in the dermal exposure model." Paustenbach cited flux values of different authors ranging from 0.05 mg/cm2-hr to 1.85 mg/cm2-hr, a difference of almost 40 fold.

It is important to remember that the flux value relied upon by Nicas in this case was based on the Hanke et al (1961) data which involved the occluded (covered) method. In a very recent paper authored by Hui, X. et al. (2009),[37] the authors concluded:

> **The effect of occlusion was significant. In this study occlusion increased absorption by 40.1 ± 24.6 times.**

Nicas applies the Hanke et al. (1961) occluded-flux data to Ben Brown's alleged solvent exposure. This application is inappropriate because the Hanke et al. (1961) occluded-flux data is not representative of Brown's actual exposures or work environment. This is a methodological error that renders the value generated by Nicas' model unreliable.

23. Nicas references the U.S. Environmental Protection Agency (EPA) as having accepted his formula. First, the EPA does not promulgate or enforce occupational health standards but estimates overall risk to various populations to agents such as benzene (by all routes of exposure, based upon 24-hours per day, 7-days per week). Second, EPA estimates generalized "risk" for a given population but does not calculate specific individual exposure risks. Third, the EPA does not use its dermal formula to convert estimates into equivalent airborne exposures – which is what Nicas has done.

It is true that the EPA has developed some dermal models for determination of risk due to exposure to pesticides and chemicals in water or soil, and they are attempting to validate these models. However, the EPA has not developed a validated dermal model for occupational exposure to benzene. OSHA, the regulating body for occupational safety and health has evaluated the dermal issue and has chosen to use an airborne exposure limit as the health standard for exposure to benzene.

24. Plaintiff states that "Nicas' methodology is thoroughly and scientifically explained in his June 15, 2009 report." It is true that Nicas attempts to validate his choice of the steady-state Hanke et al. (1961) flux value by comparing it to something else. Nicas' "validation" method is based on the idea that if his chosen Hanke et al. (1961) flux value is close to or similar to another flux value in the literature, then his methodology of selecting the Hanke et al. (1961) flux value is validated.

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37 Hui, X., Wester, R.C., Barbadillo, S, Cashmore, A and Maibach, H.I., "In Vitro Percutaneous Absorption of Benzene in Human Skin," (2009).

Nicas can find no value in the literature for comparison so he calculates one instead. Nicas turns to a paper by Modjtahedi and Maibach (2008) and converts an absorbed dose to a flux value. An analogy would be converting distance travelled to speed. In order to do this conversion, Nicas must make certain assumptions (as you would have to assume how long one travelled a certain distance in order to calculate the speed at which they travelled).[38] Nicas makes an assumption about how long the benzene remained on the skin in the Modjtahedi and Maibach (2008) paper. He chose a time value of 30 seconds. This value is not found in the paper itself, but instead, based on a personal conversation with Dr. Maibach, who stated the benzene was gone in 'under 60 seconds.'

If it is true that the benzene in the Modjtahedi and Maibach (2008) paper evaporated in just under 60 seconds, then Nicas' flux would need to be approximately reduced by one half. Nicas assumed 30 seconds, but his conversation with Dr. Maibach provided information that it was gone in 'under 60 seconds.'

Further, based on **Fick's law of diffusion**, the calculated flux by Nicas overestimates the steady-state rate at which the benzene penetrated the skin. Fick's law of diffusion states that "flux goes from regions of high concentration to regions of low concentration, with a magnitude that is proportional to the concentration gradient (spatial derivative)."[39]
Indeed, EPA calculates flux using the following equation:

[the permeability coefficient x the concentration differential across the membrane] [40]

In other words, as concentration increases in the skin due to dermal absorption, the rate at which the material passes through the skin decreases. This decrease will continue until the rate of absorption through the skin is equivalent to the rate the material is metabolized and removed from the skin (called "steady state").

The flux value Nicas calculated from Modjtahedi and Maibach, (2008) was an initial flux value and not a steady state flux value. Nicas' methodology overstates the steady-state flux because it does not take into account the decreasing concentration before steady state is reached.

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[38] distance [d] = rate [r] x time [t].

39 http://en.wikipedia.org/wiki/Fick%27s_law_of_diffusion

40 EPA, Dermal Exposure Assessment: Principles and Applications, 1992, page 4-3.

25. Plaintiff claims that I have failed to point out errors in Dr. Nicas' calculations. With respect to mathematics, Dr. Nicas stated in his report dated June 15, 2009 that Mr. Brown worked 12-hour days. In the paraffin cutting section of the report, he reported that Mr. Brown worked one-half the time away from the well head and that Mr. Brown used solvent in the well head one-half of the time. These facts indicate that 12 hours/day x ½ (away from well head) x ½ (did not use solvent) = 3 hours/day (on average) were spent on this activity where Mr. Brown was potentially exposed to paraffin cutting solvent. 3 hours per day is exactly half of the 6 hours per day assumed by Dr. Nicas. This error alone results in an overestimation of dermal absorption by 100%.

It is noteworthy that Nicas uses a linear extrapolation of pure benzene flux (provided in the Hanke et al. (1961) data) to a liquid mixture with just a few percent benzene by volume (the one allegedly used by Mr. Brown). To accomplish this mathematical extrapolation, Nicas relies on two studies involving the measure of flux for benzene in the mixture gasoline (Adami et al. (2006) and Blank & McAuliffe (1985)). If one were to apply Nicas' linear extrapolation methodology to these same studies and calculate what the flux rate would be for 100% benzene (based on the flux rates in the reports for benzene in the mixture gasoline), the resulting flux values would range from 0.139 mg/cm^2-hr to 1.05 mg/cm^2-hr. This is a seven-fold variance between the high and low value, *i.e.*, it is mere guesswork and does not pass as sound, repeatable, reliable science. The data upon which Nicas relies do not themselves support a linear extrapolation, and demonstrate a significant error in his method to determine the flux values used in his calculations.

26. The final issue is the rate of error at issue with Nicas' model. First, the EPA, upon which the Plaintiff relies for "validation" of Nicas' dermal model, states that indirect *in vivo* techniques can be used ***only for chemicals that are not volatile.***[41] Indirect techniques include the measure of the chemical remaining on the skin at the end of the exposure period, which is exactly what Hanke et al. did in their 1961 study. EPA's position is that indirect techniques cannot be used for materials like benzene, mixed solvents, etc.

Second, Plaintiff writes that the Hanke et al. (1961) paper provided enough information to conduct a statistical analysis of the data set upon which Nicas relies. While the authors do provide sufficient information to calculate precision[42,43] in the measurement of a single concentration or volume of benzene, they do not provide

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41 EPA, Dermal Exposure Assessment: A Summary of EPA Approaches, pages 4-5, 2007.

42 "Precision is basically a measure of reproducibility and is specifically defined by observing the scatter in replicate measurements." [Strobel H and Heineman W. Chemical Instrumentation: A Systemic Approach, Third Edition. Wiley-Interscience Publication, New York. 1989. p. 343.]

43 "The most useful measures of precision are the standard deviation and its square, which is called variance. Variance is the most common measure of precision, mainly because contributions to variance are additive. For that reason is it is easier to use in comparing the precision of different methods or different steps in a procedure." [Strobel and Heineman, pp 345.]

information to evaluate the accuracy[44] and precision of the method itself (method validation[45]).

Third, "standard error" is nothing more than standard deviation of the sample mean divided by the square root of the sample size. Having precision within a set of samples does not indicate that the study method accurately reflects the true value for the variable measured. Hanke et al. (1961) questioned their own method when they wrote:

> **Because of insufficient precision, which is received here for single measurements, to receive synonymous results, ...The results ... were not interpreted individually,...results of this research can be recognized, in our opinion, as entirely authentic.[46]**

Fourth, Plaintiff does not address certain methodological issues related to the work by Hanke et al (1961). For example, Hanke et al. (1961) labeled their control conditions as a "calibration," but did not indicate that they ran calibration curves for the measurement instrument, which is standard practice. Additionally, Hanke et al. (1961) adapted a colorimetric method that was utilized in their institute with less volatile compounds such as aniline and nitrobenzene, even though a validated method for quantifying benzene in air existed at the time.[47] Since that time, Hanke's method and the 1935 Bureau of Mines method have been replaced by more reliable methods, as described by Moffett et al. (1956)[48], Elkins (1959)[49], and the validated methods currently used by NIOSH[50, 51] and OSHA.[52] Finally, Hanke's method may reflect the amount of benzene

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44 "Accuracy is defined as the degree of agreement between a measured property such as concentration and the 'true value'." [Strobel and Heineman, pp 343-344.]

45 Method validation: "the protocol for experimental testing and method validation was established with a firm statistical basis. A statistical protocol provided methods of data analysis that allowed the accuracy criterion to be evaluated with statistical parameters estimated from the laboratory data. It also gave a means to evaluate precision and bias, independently and in combination, to determine the accuracy of sampling and analytical methods. [NIOSH. Research Report. Development and Validation of Methods from Sampling and Analysis of Workplace Toxic Substances. NIOSH Contract No. 210-76-0123. September 1980.

46 Hanke et al 1961 reprinted in the IJOEH page 106-107.

47 Schrenk HH, Pearce SJ, and Yant WP. "Report of Investigations: A colorimetric method for the determination of benzene." Department of the Interior, U.S. Bureau of Mines. (October 1935): R.I. 3287.

48 Maffett et al. "A Direct method for the Collection and Determination of Micro Amounts of Benzene or Toluene in Air. Industrial Hygiene Quarterly (June 1956): 186-188.

49 Elkins HB. "The Chemistry of industrial toxicology. 2nd Edition John Wiley & Sons, New York. 1959: pp 277-279 and 300-303.

50 NIOSH Manual of Analytic Methods is available at http://www.cdc.gov/niosh/nmam/ and includes validated sampling and analytical methods. OSHA validated sampling and analytical methods are available at http://www.osha.gov/dts/sltc/methods/index.html. Information regarding limit of

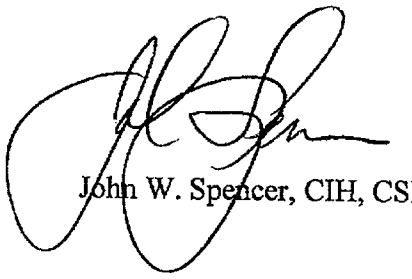
remaining under the watch glass at the end of the exposure period, but does not quantify the amount of benzene actually absorbed. The benzene no longer present under the watch glass is not equal to the amount absorbed through the skin.[53]

As shown above, Hanke et al. (1961) does not demonstrate that their modified method had sufficient sensitivity or accuracy to measure the difference between the treated (skin exposure group) and the untreated (glass exposure group). In the absence of reliable quantitation of multiple concentrations or volumes of material, one cannot know if the differences in the reported values are due to the variation in the method or true treatment differences.

Finally, as I have explained above, these questions remain: How valid, accurate, and reliable is the Hanke et al. (1961) method for estimating a flux value for a volatile compound such as benzene? How valid, accurate, and reliable is the methodology of converting that pure benzene flux value to a situation involving a highly complex mixed solvent? What is the error rate in the sampling and analytical method as used by Hanke, et al. (1961)? These are some of the questions I raised in my report, and they are absolutely essential to gauge the reliability of a dermal dose calculation.

I declare, pursuant to 28 U.S.C. §1746 and under penalty of perjury, that the statements in this Declaration are true and correct to the best of my knowledge and information.

Executed on this the 24th day of August, 2009.



John W. Spencer, CIH, CSP

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detection, range, and precision; i.e. sampling and analytical error is provided for validated NIOSH and OSHA methods

51 National Institute of Safety and Health. Method 1501 (March 2003), Method 3800 (March 2003), Method 2549 (May 1996), Method 3700 (August 1994).
http://www.cdc.gov/niosh/nmam/method-b.html (accessed 20 August 2009)

52 U.S. Department of Labor. Occupational Safety and Health Administration. "OSHA Method 1005." November 2001. http://www.osha.gov/dts/sltc/methods/validated/1005/1005.html and "OSHA Method 12." August 1980.
http://www.osha.gov/dts/sltc/methods/organic/org012/org012.html (accessed 20 August 2009)

53 Johnson HL. "Systematic Absorption of Benzene: Evaluation of experimental data and comparison of dermal and inhalation exposure. (19 July 1979) OSHA Docket H059B, Exhibit 143-2c.